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10/551,690	02/17/2006	Tero Soukka	TUR-172	8006

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EXAMINER	
YU, MELANIE J	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,690	SOUKKA ET AL.	
	Examiner	Art Unit	
	MELANIE YU	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's arguments filed 23 December 2009 have been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. Claim 26, 27, 29 and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kameda et al. (US 4,959,306) in view of Willner et al. (US 7,135,295, claims priority to PCT/IL00/00048, which was published in English).

Kameda et al. teach a nanoparticle comprising:

a self-assembling shell built up of several protein subunits of one type (apoferritin contains 24 protein subunits and is arranged as a spherical shell, which is a particle, col. 8, lines 65-67, although Kameda et al. do not specifically recite the particle being a nanoparticle, the particle is the same type, apoferritin, as that described in the instant specification and is therefore also a nanoparticle) assembled in an organized

manner to form the shell having an inner surface facing the inside and an outer shell facing the outside of the particle (iron is removed from ferritin, which indicates that a portion of the apoferritin faces the inside of the shell and an outer portion faces the outside of the particle, col. 10, lines 38-48),

wherein one of the types of subunits have a first binding moiety facing the outside of the particle for binding of any specific ligand binding protein (linkers specific to ferritin conjugated to apoferritin, col. 10, lines 55-68); and

the particle contains attached to a type of subunit having a second binding moiety for binding a marker (Fab' fragments are labeled with fluorescein and attached to the particle, col. 11, lines 1-32); and

the marker enables detection of the particle (fluorescein is used for detection, col. 11, lines 49-52) wherein the shell of the nanoparticle is an apoferritin-like particle (col. 8, lines 65-67).

Kameda et al. do not specifically teach a genetically fused first binding moiety and a genetically fused second binding moiety.

Willner et al. teach a protein attached to a binding ligand, through either conjugation by chemical binding or forming a fusion protein by means of genetic engineering (col. 9, lines 41-48), in order to provide a synthetic macromolecule that has a binding domain with an affinity for the analyte.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to attach the binding moieties to the subunits in the invention of Kameda et al., by genetic fusion as taught by Willner et al. One having

ordinary skill in the art would have been motivated to make such a change as a mere alternative and functionally equivalent attachment technique and since the same expected attachment between a protein and a binding moiety would have been obtained. The use of alternative and functionally equivalent techniques would have been desirable to those of ordinary skill in the art based on the economics and the availability of equipment and components to form an attachment between a binding moiety and protein.

Regarding claim 27, Kameda et al. teach the first binding moiety fused to the N-terminus of the apoferritin protein (linkers are attached to the end of the apoferritin and therefore are fused to the N-terminus, col. 10, lines 55-68).

With respect to claim 29, Kameda et al. teach the marker being fluorescein (col. 11, lines 1-32).

Regarding claim 36, Kameda et al. teach an apoferritin that is produced from a human liver ferritin (col. 10, lines 38-48), but do not recite the size of the apoferritin. However, the instant specification teaches an apoferritin produced from a human liver ferritin molecule in the background of the invention as having the necessary dimensions. Therefore, the apoferritin molecule of Kameda et al. meets the recited size requirements as indicated by the instant specification.

With respect to claim 37, Kameda et al. teach the number of subunits being 24 (col. 8, lines 65-67), which encompasses the recited range of more than 8.

Regarding claim 38, Kameda et al. teach the nanoparticle of claim 1 and therefore teach a kit comprising the particle.

3. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kameda et al. (US 4,959,306) in view of Willner et al. (US 7,135,295), as applied to claim 26, in view of Bertozzi et al. (US 6,713,274).

Kameda et al. in view of Willner et al. teach an apoferritin nanoparticle having a fluorescent marker that is fluorescein, but fail to specifically teach the marker being a lanthanide.

Bertozzi et al. teach that a detectable fluorescent marker may alternatively be fluorescein, luciferase or a lanthanide that is ^{124}Eu (col. 10, lines 11-27), in order to provide a detectable label for detection of antibody binding.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to substitute for the fluorescein marker taught by Kameda et al. in view of Willner et al., a luciferase or lanthanide marker as taught by Bertozzi et al. One having ordinary skill in the art would have been motivated to make such a change as a mere alternative and functionally equivalent labeling technique and since the same expected detection effect would have been obtained. The use of alternative and functionally equivalent techniques would have been desirable to those of ordinary skill in the art based on the economics and availability of components.

4. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kameda et al. (US 4,959,306) in view of Willner et al. (US 7,135,295), as applied to claim 26, in view of Griffiths et al. (US 2003/0124586).

Kameda et al. in view of Willner et al. teach an apoferritin having two types of binding moieties, but fail to teach a third type of binding moiety facing the outside of the particle for binding to a solid support.

Griffiths et al. teach a binding moiety facing the outside of an apoferritin for binding to a solid support (par. 239), in order to provide linkage of a probe and target analyte to a substrate for detection.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to add onto the apoferritin nanoparticle of Kameda et al. in view of Willner et al., a third binding moiety facing the outside of the particle for binding to a solid support as taught by Griffiths et al., in order to provide detection of binding that is localized to a specific area.

5. Claims 28 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kameda et al. (US 4,959,306) in view of Willner et al. (US 7,135,295), as applied to claim 26, in view of Chandler et al. (US 6,599,331).

Kameda et al. in view of Willner et al. teach a first and second binding moiety, but fail to teach the first binding moiety being protein A, protein G, protein L CBP or BCCP.

Chandler et al. teach that protein A is conjugated to a particle for attachment of a fluorescent label (col. 7, lines 42-65), in order to provide labeling or specific binding for a bead.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include as the first binding moiety of Kameda et al. in

view of Willner et al., a protein A conjugated to the particle as taught by Chandler et al., in order to provide sufficient and easy attachment of labels to the particle.

6. Claims 33, 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kameda et al. (US 4,959,306) in view of Willner et al. (US 7,135,295), as applied to claim 26, in view of Bergmann et al. (US 6,537,760).

Kameda et al. in view of Willner et al. teach the first and second binding moiety being an antibody against CRP, ABO blood group antigens and TSH.

Bergmann et al. teach an antibody against TSH as a first specific binding moiety or to bind a label (antibody to TSH is immobilized to a particle and binds to TSH to detect a labeled TSH, col. 9, lines 5-12), in order to provide accurate detection of TSH.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to substitute the first or second moiety of Kameda et al. in view of Willner et al., an antibody to TSH as taught by Bergmann et al., in order to provide an accurate indicator with greater clinical value for TSH which is detected to diagnose Graves' disease.

With respect to claim 36, a nanoparticle having these binding moieties and an apoferritin shell is the same as that recited in the claims and would therefore have the same size and radius properties as those recited in claim 36. Therefore, according to the instant specification, the nanoparticle taught by Kameda et al. in view of Bergmann et al. has a radius that is between 10 and 40 nm.

7. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kameda et al. (US 4,959,306) in view of Willner et al. (US 7,135,295), as applied to claim 26, in view of Oon et al. (US 2003/0077578).

Kameda et al. in view of Willner et al. teach a first and second binding moiety, but fail to teach the second binding moiety being protein A, protein G, protein L CBP or BCCP.

Oon et al. teach that protein A is conjugated to a support as a specific binding moiety (par. 96), in order to provide an antibody that binds immunoglobulins.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to substitute as the first binding moiety of Kameda et al. in view of Willner et al., a protein A conjugated to the particle as taught by McCormick et al., in order to separate any tagged target protein complexes from a sample for accurate detection.

Response to Arguments

1. Applicant's arguments filed 23 December 2009 have been fully considered but they are not persuasive.

2. At pages 1-3, applicant argues that Kameda et al. fail to disclose the genetically fused first binding moiety of the claimed recombinant nanoparticle and instead chemically binds its binding moieties to ferritin subunits which produce a random distribution of binding moieties. Applicant argues that this differs from the instant claims because the genetically fused first binding moieties produce apoferritin that are identical

to one another in that the binding moieties are located at the same place in the subunit's polypeptide chain.

Applicant's argument is not persuasive because Kameda et al. is not relied upon for teaching the genetically fused first binding moieties, which produces a product different from the chemical fusion used by Kameda et al. Willner et al. is relied upon for teaching the limitation of genetically fused first binding moieties.

3. At pages 3, in response to applicant's argument that Willner et al. is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Willner et al. teach different types of attachment of a first binding moiety to a protein, which is relevant to the instant claims because the instant claims involve attaching a binding moiety to a specific type of protein.

4. At page 4, applicant argues that Willner et al. do not teach the advantages or disadvantages of a chemical binding or genetic fusion attachment technique and that Willner et al. fail to teach any suggestion to prepare recombinant apoferritin particles from genetically fused binding moieties. Applicant argues that the chemical conjugation and genetic fusion are not functionally equivalent because chemical conjugation produces a heterogeneous reaction product and genetic fusion produces a homogeneous reaction product.

Applicant's argument is not persuasive because Willner et al. teach that either chemical binding or genetic fusion may be used to attach a binding moiety to a protein. The phrase "functionally equivalent attachment techniques" is not used in the rejection to imply that the attachment methods yield the exact same product, but rather to acknowledge that the attachment methods yield products that function the same. Therefore one having ordinary skill in the art would recognize that genetic fusion would be an acceptable alternative to the chemical binding for attaching a binding moiety to the apoferritin taught by Kameda et al. since Willner et al. teach both chemical binding and genetic fusion for attachment of a binding moiety to a protein.

5. At page 5, applicant argues that Willner et al. fail to teach the production of a recombinant apoferritin particle and only shows formation of a fusion protein through engineering techniques, and therefore improper hindsight reasoning was employed to combine an isolated disclosure in Willner et al. with Kameda et al.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Willner et al. teach both the chemical conjugation used for attachment by Kameda et al. and genetic fusion recited in the instant claims, and therefore provides

the proper nexus required for obviousness as described above, without employing improper hindsight reasoning.

6. With respect to applicant's arguments regarding the combination of Kameda et al. and Willner et al. with Bertozzi et al., Griffiths et al., Chandler et al., Bergmann et al. and Oon et al., applicant's arguments are not persuasive for the reasons addressed in the arguments of Kameda et al. and Willner et al. above.

Conclusion

7. No claims are allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELANIE YU whose telephone number is (571)272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Melanie Yu/
Primary Examiner, Art Unit 1641